# Association between Essential Tremor and Blood Lead Concentration

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**Lead is a ubiquitous toxicant that causes tremor and cerebellar damage. Essential tremor (ET) is a highly prevalent neurologic disease associated with cerebellar involvement. Although environmental toxicants may play a role in ET etiology and their identification is a critical step in disease prevention, these toxicants have received little attention. Our objective was to test the hypothesis that ET is associated with lead exposure. Therefore, blood lead (BPb) concentrations were measured and a lifetime occupational history was assessed in ET patients and in controls. We frequency matched 100 ET patients and 143 controls on age, sex, and ethnicity. BPb concentrations were analyzed using graphite furnace atomic absorption spectrophotometry. A lifetime occupational history was reviewed by an industrial hygienist. BPb concentrations were higher in ET patients than in controls (mean ± SD, 3.3 ± 2.4 and 2.6 ± 1.6 μg/dL, respectively; median, 2.7 and 2.3 μg/dL; $p = 0.038$). In a logistic regression model, BPb concentration was associated with diagnosis [control vs. ET patient, odds ratio (OR) per unit increase = 1.21; 95% confidence interval (CI), 1.05–1.39; $p = 0.007$]. BPb concentration was associated with diagnosis (OR per unit increase = 1.19; 95% CI, 1.03–1.37; $p = 0.02$) after adjusting for potential confounders. Prevalence of lifetime occupational lead exposure was similar in ET patients and controls. We report an association between BPb concentration and ET. Determining whether this association is due to increased exposure to lead or a difference in lead kinetics in ET patients requires further investigation.** *Key words:* **epidemiology, essential tremor, etiology, lead, occupational exposure.** *Environ Health Perspect* **111:1707–1711 (2003). doi:10.1289/ehp.6404 available via** *http://dx.doi.org/* **[Online 3 July 2003]**

Essential tremor (ET) is a neurologic disease that is characterized by an action tremor of the hands and/or head. Patients also may have signs of more widespread cerebellar involvement (e.g., intention tremor, ataxia; Deuschl et al. 2000; Singer et al. 1994; Stolze et al. 2000), abnormalities referable to the basal ganglia (e.g., rest tremor, subclinical signs of bradykinesia; Cohen et al. 2003; Rajput et al. 1993), and cognitive deficits (Gasparini et al. 2001; Lombardi et al. 2001). ET is considered to be distinct from age-related enhanced physiologic tremor, which has different clinical and electrophysiologic features (Louis et al. 1997; Louis and Pullman 2001). The disease is highly prevalent in the general population (1–6%) (Louis et al. 1998b; Rautakorpi et al. 1982) and occurs in all populations studied to date (Hornabrook and Nagurney 1976; Louis et al. 1998b). The prevalence increases with age. Estimates of the prevalence in individuals who are in their sixties and seventies have been as high as 20.5% (Khatter et al. 1996). As such, ET is one of the most common neurologic diseases. The pathogenesis of this progressive (Louis et al. 2003) and often disabling (Louis et al. 2001a) disease is poorly understood, although there is evidence of cerebellar involvement (Bucher et al. 1997; Louis et al. 2002a; Wills et al. 1994). There is no cure for ET, and there has been no attempt to favorably modulate or halt its progression with neuroprotective therapy. Medical treatment merely aims to lessen the severity of the tremor, which is the major symptom, and the first-line medications are ineffective in up to 50% of patients (Gironell et al. 1999; Louis and Greene 2000; Sasso et al. 1990).

Although genetic susceptibility is an important determinant of disease etiology (Louis et al. 2001b; Tanner et al. 2001), it has been hypothesized that nongenetic factors (i.e., environmental factors such as toxicants) could contribute to disease etiology in many cases (Louis 2001; Louis et al. 2002b; Tanner et al. 2001). The identification of these factors is a critical step in disease prevention, yet they have received little attention (Louis 2001).

Lead is a ubiquitous toxicant (Konat and Clausen 1974; Schroeder and Tipton 1968), and laboratory animals and humans exposed to high levels of either inorganic or organic forms of lead develop neurologic disorders in which action tremor is prominent (Booze et al. 1983; Coulehan et al. 1983; Goldings and Stewart 1982; Konat and Clausen 1974; Seshia et al. 1978; Valpey et al. 1978; Young et al. 1977). Destruction of cerebellar Purkinje cells is a major feature of the pathology of lead toxicity (Valpey et al. 1978). The effect of chronic, low-level exposure to lead has been linked with developmental problems, deficits in intellectual performance and decreased stature in children (Brody et al. 1994), and poorer performance on cognitive tests in adults (Muldoon et al. 1993; Payton et al. 1998).

To test the hypothesis that ET is associated with lead exposure (Louis 2001), we assessed *a*) blood lead (BPb) concentrations and *b*) lifetime occupational history in ET patients and in control subjects who were enrolled in a study of the environmental epidemiology of ET.

## Materials and Methods

*Participants.* ET patients were cared for by neurologists at the Neurological Institute of New York, Columbia-Presbyterian Medical Center (CPMC) (Louis et al. 2002b). They were identified from a computerized database listing patients billed within the last 3 years supplemented by a computerized database at the Center for Parkinson's Disease and Other Movement Disorders, CPMC, which listed patients seen within the last 10 years. All patients had received a diagnosis of ET from their treating neurologist at the institute. ET patients were selected for enrollment in a study of the environmental epidemiology of ET. Office records were reviewed and patients with physical signs or diagnoses of dystonia, parkinsonism (rigidity, bradykinesia), or spinocerebellar ataxia were excluded. The CPMC internal review board approved of all study procedures, and written informed consent was obtained at the time of enrollment.

Controls were identified from the New York metropolitan area using random-digit dialing. These controls were frequency matched to CPMC patients based on 5-year age strata, sex, and ethnicity.

Patients and controls were contacted; 77.2% of patients and 57.0% of controls agreed to participate. Enrollees were similar to refusers in terms of age (68.0 ± 10.0 vs. 66.8 ± 16.7 years; mean ± SD), sex (54.7% vs. 54.2% female), race (90.1% vs. 86.1% white), and education (14.7 ± 4.0 vs. 14.6 ± 3.6 years; all $p > 0.05$).

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